REMARKS/ARGUMENTS

Claims 1-20 are pending. A substitute Sequence Listing and corresponding CRF is provided. No changes have been made to any of the sequences, though minor edits have been made to name the individual inventors, conform the title to the ADS, and indicate the presence of 4 sequences. The CHECKER program indicated "No errors". Support for the amendment of claim 1 is found on page 1 and at the bottom of page 8 of the specification. New claim 12 finds support on page 7 at [0014]. Claims 13-15 find support at page 8, line 5. Claims 16-20 find support on page 8, line 15 *ff*. No new matter has been added. Favorable consideration of this amendment and allowance of this case are respectfully requested.

The Applicants thank Examiners Wang and Saoud for the courteous and helpful interview of December 9, 2008. The Applicants were encouraged to show that "PTX3" was a term well-recognized in the art and further describe how the "grade" (which was viewed as indefinite and relative) or relative extent of vascular injury can be determined. The disclosure at the bottom of page 8 which refers to various ways to measure the extent of vascular injury was discussed. The Applicants were encouraged to identify "PTX3" using a sequence identifier or point out that the PTX3 designation was well-known in the art and would unambiguously identify this type of protein. Ways to avoid the rejections of record were discussed based on comparison of the extent of vascular injury were discussed.

Objection—Sequence Listing

The disclosure was objected to as not containing the Sequence Listing in computer readable form (CRF). This objection is moot in view of the attached substitute Sequence Listing.

Sequence Listing Statement

As required by 37 C.F.R. 1.821(f), the sequence information recorded in the computer-readable form (CRF) of the substitute Sequence Listing is identical to that in the paper copy of the substitute Sequence Listing; or if this substitute Sequence Listing is electronically-filed, then the sequences in the electronically filed Sequence Listing are identical to the sequences disclosed in this application. Pursuant to 37 C.F.R. 1.821(g) the Applicants state that no new matter has been introduced.

Objection—Claim 1

Claim 1 was objected to for reciting "PTX3". This issue is moot in view of the amendment of claim 1. However, the Applicants point out that "PTX3" is a designation not an abbreviation. This designation is well-known in the art as shown by the title of Fazzini, et al., Arthritis and Rheumatism 44(12):2841 (2001) and Latini, et al., XP008083208 (see title also), and Breviorio, et al., J. Biol. Chem. 267(31):22190 (1992).

Objection—Claims

Claims 4-7 were objected to as being improper multiple dependent claims. This issue is now moot.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-3 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite as omitting essential steps. This rejection is moot in view of the amendments above.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-3 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because claim 1 recites "a grade" and for use of the term "PTX3". This rejection is moot in view of the amendment above and explanation that PTX3 was a well-known designation as of the filing date, not an abbreviation.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-3 were rejected under 35 U.S.C. 112, first paragraph, as only being enabled for diagnosis of coronary artery condition (CA), unstable angina (UAP) and myocardial infarction (MCI) by measuring increased PTX3 using an antibody-based assay as compared to a control. This rejection is moot in view of the amendments to claim 1. Immunoassays useful for measuring PTX3 levels were known in the art as shown by Peri, et al., Circulation 102: 636-641 (2000) or Latini, et al. US 2004/0137544 A1 [0009]. Accordingly, one of skill in the art would have been able to measure PTX3 using the claimed methods.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-3 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description on the ground that the specification only shows possession of the concept of diagnosis of coronary artery condition (CA), unstable angina (UAP) and myocardial infarction (MCI) by measuring increased PTX3 using an antibody-based assay as compared to a control. Page 10, line 4 of the Official Action ("OA") indicates that "Applicant is not in possession of detecting other vascular injury or heart diseases or cerebrovascular diseases".

Page 8, line 15 *ff.* of the specification disclose:

> In the present invention, vascular injury includes vascular injury caused by hyperlipidemia, cerebral disease, hypertension, diabetes, obesity, and smoking.

The surrounding text on pages 8 and 9 clearly disclose all types of vascular injury characterized by various histological phenomena. General methods for measuring PTX3 levels (not limited to antibody-based methods) are described on page 6, lines 3-5 and in the original claims. The original claims also describe the general concept of determining the extent or grade of vascular injury by measuring PTX3 levels (see e.g., claim 1). As evident from these portions of the specification, the Applicants clearly possessed the concept of assessing vascular injuries other than CA, UAP and MCI. Therefore, the Applicants clearly were in possession of the concept of treating vascular injury not limited to CA, UAP and MCI. Therefore, this rejection cannot be sustained.

Rejection—35 U.S.C. §102

Claims 1-3 were rejected under 35 U.S.C. §102(b) as being anticipated by Peri, et al., Circulation 102:636. Peri is directed to a method using PTX3 as an early indicator of myocardial infarction (MCI), but does not suggest using this marker to assess the extent of vascular injury as determined by the criteria described in claim 1. As disclosed on page 52 of the specification "PTX3 serves as a marker highly specific to the blood vessel and is not a marker for the diagnosis of systemic inflammation". Moreover, new claims 16-17 exclude methods using test samples from subjects having MCI. Accordingly, this rejection cannot be maintained.

Rejection—35 U.S.C. §102

Claims 1-3 were rejected under 35 U.S.C. §102(a) and (e) as being anticipated by Latini, et al., U.S. 2004/0137544. Latini is directed to a "method for the early determination of the risk of death or heart failure in infarction patients" or patients with cerebral ictus (see abstract) or as a "prognostic marker in cardiovascular and cerebrovascular diseases" [0001].

Latini does not suggest using a marker to assess the extent of vascular injury as determined by the criteria described in claim 1. Moreover, Latini does not contemplate obtaining test samples from subjects not having AMI (myocardial infarction) or ictus and would not apply to claims such as 19 and 20. Accordingly, this rejection cannot be maintained.

Rejection—35 U.S.C. §102

Claims 1-3 were rejected under 35 U.S.C. §102(a) as being anticipated by Latini, et al., Circulation 110:2349. Latini describes a method of determining a myocardial infarction patient's prognosis after several months from the time of the assay of a biological sample from the patient. On the other hand, the present invention immediately assesses the extent of vascular injury at the time of the assay, not months afterward.

Latini, page 2350, 3rd and 4th paragraphs, cited on page 14 of the OA refers to "Comparative predictivity of PTX3" with respect to various outcomes including all-cause death, heart failure, cardiac residual ischemia of "patients with acute coronary syndromes" (page 2350, 1st col., line 14). Page 2352, first full paragraph, indicates that "Compared with other biomarkers. . .PTX3 has been shown to be an earlier and stronger **prognostic** marker of death in . . .patients with MI [myocardial infarction]".

As apparent from the excerpts above, Latini involves use of PTX3 as a **prognostic** marker for disease outcomes in subjects having acute coronary syndromes, but **not as a marker to assess the extent of vascular injury**. Accordingly, it does not anticipate the present claims and this rejection may now be withdrawn.

Provisional Rejection--Obviousness-type Double Patenting

Claims 1-3 were rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1-3 of copending U.S. Application 12/092,272. The Applicants

submit that the foregoing amendments and remarks address all the remaining rejections and place this application in condition for allowance. Accordingly, this provisional double patenting rejection can be withdrawn since the copending application has not yet been allowed, MPEP 804(I)(B).

Conclusion

In view of the amendments and remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

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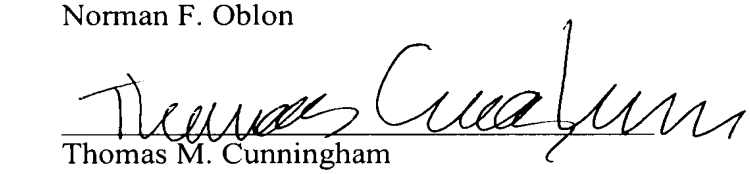

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